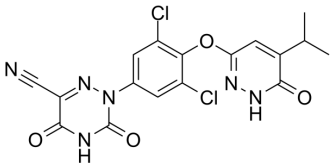
Resmetirom

Cat. No.:	HY-12216
CAS No.:	920509-32-6
Molecular Formula:	$C_{17}H_{12}Cl_2N_6O_4$
Molecular Weight:	435.22
Target:	Thyroid Hormone Receptor
Pathway:	Vitamin D Related/Nuclear Receptor
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : 75 mg/mL (172.33 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2977 mL	11.4884 mL	22.9769 mL
	5 mM	0.4595 mL	2.2977 mL	4.5954 mL
	10 mM	0.2298 mL	1.1488 mL	2.2977 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 3.75 mg/mL (8.62 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 3.75 mg/mL (8.62 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 3.75 mg/mL (8.62 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Resmetirom (MGL-3196) is a highly selective and orally active thyroid hormone receptor β (THR-β) agonist with an EC_{50} value of 0.21 μM. Resmetirom can be used for the study of noncirrhotic nonalcoholic steatohepatitis[1].

IC_{50} & Target

EC50: 0.21 μM (THR-β)[1]

In Vitro

Resmetirom (MGL-3196) is 28-fold selective for THR-β (EC_{50}=0.21 μM) over THR-α (EC_{50}=3.74 μM) in a functional assay. Resmetirom (MGL-3196) shows an IC_{20} of roughly 30 μM for blockage of the hERG channel. The IC_{50} for CYP3A4/5 and for

	CYP2C19 is >50 μM, and there is only weak inhibition (roughly 22 μM) of CYP2C9[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Resmetirom (MGL-3196) exhibits good exposures and reasonable oral bioavailability in rats. The volume of distribution and clearance are both low. Dose proportional increases in exposure are observed for a suspension of Resmetirom (MGL-3196) given orally to DIO mice[1].In animals treated with Resmetirom (MGL-3196) there is a reduction in cholesterol and in liver size, which is secondary to reduction of liver TG. There is no effect on bone mineral density (BMD) or heart or kidney size in Resmetirom (MGL-3196) treated animals[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Animal Administration [1]	Rats[1] Resmetirom (MGL-3196), compounds 54 and 55 are formulated in 4% DMSO, 15% PEG-400, and 81% of 30% HPBCD in phosphate buffer and are administered intraperitoneally. For MGL-3196 and 54, 4 rats per group are tested at 5, 20, and 37.5 mg/kg. For 55, 3 rats per group are tested at 5 and 15 mg/kg and 4 rats are tested at 50 mg/kg[1]. Mice[1] Six week old C57Bl/6J mice are placed on a high fat diet for 34 weeks. At day 0, 9 mice per group are treated daily doses by gavage with vehicle (2% Klucel LF, 0.1% Tween 80 in water) or 0.3, 1, 3, or 10 mg/kg Resmetirom (MGL-3196) for 23 days. In a parallel study, at day 0, 9 mice per group are treated with daily doses of vehicle (Dulbecco's phosphate buffered saline, pH adjusted to 9.0 with 1 N NaOH) or 10, 30, or 100 μg/kg T3[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Nat Metab. 2024 Nov 22.
- Br J Pharmacol. 2021 Jun;178(12):2412-2423.
- Acta Physiol. 2024 Aug 16:e14217.
- Nutrients. 2024 Dec 10;16(24):4260.
- Biochem Biophys Res Commun. 2024 Sep 24:734:150742.

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REFERENCES

[1]. Kelly MJ, et al. Discovery of 2-[3,5-dichloro-4-(5-isopropyl-6-oxo-1,6-dihydropyridazin-3-yloxy)phenyl]-3,5-dioxo-2,3,4,5-tetrahydro[1,2,4]triazine-6-carbonitrile (MGL-3196), a Highly Selective Thyroid Hormone Receptor β agonist in clinical trials for the treatment of dyslipidemia. J Med Chem. 2014 May 22;57(10):3912-23.

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